Amendments to the Specification

Please delete page 89 and add new figure 33.

At the indicated page and line numbers, please add the following paragraph:

(Page 22, line 3) Fig. 33 is a diagram showing the biosynthesis of a ketolide.

At the indicated page and line numbers, please replace the existing section, paragraph, or paragraphs with the following section, paragraph, or paragraphs:

(Page 20, lines 23 through 24)
~~Fig. 10 a and b is~~ Figs. 10A, 10B, and 10C constitute a diagram showing the construction of plasmid pIG1;

(Page 20, lines 27 through 30)
~~Fig. 12 is~~ Figs. 12A and 12B constitute a diagram showing the construction of plasmid pKW15; this includes DNA encoding a loading module, a first extender module, and the chain-terminating thioesterase, capable of receiving modules;

(Page 20, lines 33 through 34)
~~Fig. 14 is~~ Figs. 14A, 14B, 14C, and 14D constitute a diagram showing the construction of plasmid pAR8;

(Page 87, line 35 through page 88, line 12)
S. erythrea NRRL2338/pKETO was inoculated into sucrose-succinate medium containing 10 μg/ml thiostrepton and allowed to grow for four days at 30°C. After this time the broth is filtered to remove mycelia, the supernatant adjusted to pH 9.5 and then extracted twice with equal volumes of ethyl acetate. The combined ethyl acetate extracts were evaporated to dryness, the residue taken up in methanol (5 ml) and then

analysis by HPLC and electrospray MS. It is found that the major product is the expected 3-ketolide in an approximate yield of 10 mg/ml. Analysis of the electrospray mass spectrum shows that the proton adduct for this compound displays a MH^+ mass of 558.4, which was confirmed by accurate mass analysis; MH^+ requires 558.36418 $C_{29}H_{52}O_9N$, observed 558.36427 (Fig. 33).

(Page 93, line 20 through page 94, line 26)
S. coelicolor CH999/pMO7 was inoculated into YEME medium containing 50 _g/ml thiostrepton and allowed to grow for five days at 28-30%C. After this time the broth was filtered to remove mycelia and the pH was adjusted to pH 3. The broth was extracted twice with two volumes of ethyl acetate and the combined ethyl acetate extracts were washed with an equal volume of saturated sodium chloride, dried over anhydrous sodium sulphate, and the ethyl acetate was removed under reduced pressure, to give about 200 mg crude product. This was digested with 2 ml of methanol, and mixed with 0.5 g of dry silica gel, and then subjected to flash chromatography on a column of the same material (1 cm x 15 cm) The column was eluted with diethyl ether, and fractions of 10 ml each were collected. Fractions 4-8 were pooled, and the diethyl ether was evaporated to leave about 10 mg of oily residue containing the compound of interest. These were purified further by hplc on an octadecylsilica reverse phase column (10 mm x 25 cm) eluted at a flow rate of 2 ml/minute with an isocratic mixture of water/methanol 75:25 (vol/vol) for five minutes, then with a linear gradient of increasing methanol, reaching water/methanol 55/45 (vol/vol) after 30 minutes. After about 11 minutes, fractions were collected containing, as the minor component (Ac)4-nor-TKL (R_1=Me, R_2=H, R_3=Me) and after about 18 minutes fractions were collected containing, as the major component, 4-nor-TKL (R_1=Me, R_2=H, R_3=Et).

The ^1H spectrum of 4-nor-TKL was determined using a Bruker AM-

400 NMR spectrometer. Found: (400 MHz, $CDCl_3$) 4.18 (1H, dtd, 11.8, 6.1, 2.9 Hz, H-5), 3.75 (1H, ddd, 11.0, 10.0, 4.0 Hz, H-3), 2.35 (1H, dq, 10.0, 7.0 Hz, H-2), 2.20 (1H, ddd, 13.3, 4.0, 2.9 Hz, H-4eq), 1.6 - 1.88 (3H, m, 2xH-g, H-4ax), 1.41 (1H, d, 7.0 Hz, CH3-3'), 1.01 (1H, t, 7.5 Hz, CH3-7) ppm.